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Factors Associated with Poor Outcomes among Hospitalized Patients with COVID-19: Experience from a MERS-CoV Referral Hospital

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Factors Associated with Poor Outcomes among Hospitalized Patients with COVID-19: Experience from a MERS-CoV Referral Hospital

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Abstract

Background: Coronavirus disease 2019 (COVID-19) has resulted in millions of deaths, including more than 6000 deaths in the Kingdom of Saudi Arabia (KSA). Identifying key predictors of intensive care unit (ICU) admission and mortality among infected cases would help in identifying individuals at risk to optimize their care. We aimed to determine factors of poor outcomes in hospitalized patients with COVID-19 in a large academic hospital in Riyadh, KSA that serves as a Middle East Respiratory Syndrome coronavirus (MERS-CoV) referral center.

Methods: This is a single-center retrospective cohort study of hospitalized patients between March 15 and August 31, 2020. The study was conducted at King Saud University Medical City (KSUMC). COVID-19 infection was confirmed using real-time reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-COV-2. Demographic data, clinical characteristics, laboratory, radiological features, and length of hospital stay were obtained. Poor outcomes were, admission to ICU, need for invasive mechanical ventilation (IMV), and in-hospital all-cause mortality.

Results: Out of 16,947 individuals tested in KSUMC, 3,480 (20.5%) tested positive for SARS-CoV-2 and of those 743 patients (21%) were hospitalized. There were 62% males, 77% were younger than 65 years. Of all cases, 204 patients (28%) required ICU admission, 104 (14%) required IMV, and 117 (16%) died in hospital. In bivariate analysis, multiple factors were associated with mortality among COVID-19 patients. Further multivariate analysis revealed the following factors were associated with mortality: respiratory rate more than 24/min and systolic blood pressure < 90 mmHg in the first 24 hours of presentation, lymphocyte count $<1 \times 10^9$/L and aspartate transaminase level > 37 units/L in the

first 48 hours of presentation, while a RT-PCR cycle threshold (Ct) value ≤24 was a predictor for IMV.

Conclusion: Variable factors were identified as predictors of different outcomes among COVID-19 patients. The only predictor of IMV was a low initial Ct values of SARS-CoV-2 PCR. The presence of tachypnea, hypotension, lymphopenia, and elevated AST in the first 48 hours of presentation were independently associated with mortality. This study provides possible independent predictors of mortality and invasive mechanical ventilation. The data may be helpful in the early identification of high-risk COVID-19 patients in areas endemic with MERS-CoV.

Keywords: COVID-19, Risk Factors, ICU, invasive mechanical ventilation

1. Introduction:

As of February 2021, just over one year has passed since the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first discovered. This virus is the cause of the coronavirus disease 2019 (COVID-19) pandemic, which has infected almost 100 million people worldwide with almost two million deaths[1]. It has caused almost 370,000 cases with > 6,000 deaths in the Kingdom of Saudi Arabia (KSA)[2]. Thus, potential predictors of COVID-19-related mortality among different populations should be investigated to help optimize patient care and appropriately utilize health care resources[3].

Recent reports from several countries have suggested that older age, male gender, history of heart disease[3, 4], and baseline chronic conditions[5] are significantly associated with poor outcomes. Hypertension (HTN) is associated with poor outcomes, and anticoagulant treatment may be associated with clinical benefits in terms of survival in patients with COVID-19[6]. Thus, identifying predictors of poor outcomes across different populations is essential. In KSA, limited studies have investigated the predictors of morbidity and mortality in patients with COVID-19. A retrospective study of 352 critically ill patients with COVID-19 in KSA showed various predictors of 28-day mortality including old age, active smoking, increased lactate and D-dimers[7], similarly another study from Mecca showed that advanced age, end-stage renal disease, low oxygen saturations and high D-dimers were all associated with mortality[8]. A case series of 768 patients at a single center in Riyadh revealed that lung disease, obesity, smoking, diabetes mellitus were all predictors of intensive care admission[9], while another study from Madina showed higher mortality odds in older groups above 65 years with high C-reactive protein[10]. Within the same region, a study from Oman in-hospital mortality was associated with older age, heart disease, liver disease, high

ferritin, and patients requiring intensive care admission[11], while a study from Kuwait age above 50 years, smoking, elevated C-reactive protein and elevated procalcitonin levels were all associated with admission to intensive care[12].

In addition, KSA is currently the only country in the world where Middle East Respiratory Syndrome Coronavirus (MERS-CoV) still causes sporadic community cases[13] and nosocomial outbreaks[14]. Therefore, we aimed to study numerous cases and investigate their clinical and laboratory predictors for poor outcomes.

2. Methodology:

2.1. Design, inclusion, and exclusion criteria:

This work is a retrospective cohort single-center study carried out at King Saud University Medical City (KSUMC) in Riyadh, Saudi Arabia, which serves as a MERS-CoV referral hospital. During the study period from March 15 to August 31, 2020, we included patients aged 18 years or older who tested positive for SARS-CoV-2 infection and required hospitalization for at least 24 hours. Patients who were still hospitalized by the last day of study inclusion were followed until discharge or in-hospital mortality, with the last outcome monitored until October 15, 2020. We aimed to study factors associated with a poor outcome, which is defined as: admission to the intensive care unit (ICU), the use of invasive mechanical ventilation (IMV), or in hospital all-cause mortality.

Based on the definition of severity by the Saudi Ministry of Health [15], disease severity was classified into asymptomatic, upper respiratory tract infection (URTI), mild to moderate disease (i.e., no oxygen requirement, no clinical evidence of pneumonia but with other symptoms, such as fever and diarrhea), severe disease (in which oxygen therapy was needed), and critical cases (in which acute respiratory distress syndrome, overt sepsis, an altered level of consciousness, or

multiorgan dysfunction were documented). All patients were admitted to single rooms under droplet and contact precautions as per hospital policy. They were placed in airborne infection isolation rooms with 6–12 air changes per hour, or, when not available, in a single room with high-efficiency particulate air filter. If aerosol-generating medical procedures were required, healthcare workers (HCWs) used fit-tested N95 masks. The study was approved by the Institutional Review Board of the KSUMC (IRB# E20-4979).

2.2. Laboratory testing:

All the hospitalized patients underwent a nasopharyngeal or throat swab upon admission. The swabs were sent in viral transport media (Copan, Brescia, Italy). A confirmed COVID-19 was based on a positive result for both SARS-CoV-2 *E* and *S* genes using the RealStar® SARS-CoV-2 real-time reverse transcriptase PCR (RT-PCR) kit (Altona-Diagnostics, Hamburg, Germany) and Rotor-gene Q system (Qiagen®, Santa Clarita, CA, USA).

2.3. Data collection:

Patient data, which included demographic data, previous and current medical history, clinical findings, vital signs upon admission, laboratory results (i.e., molecular tests, microbiological tests), and radiological investigations (i.e., chest X-rays (CXR), computed tomographic scans), were collected directly from electronic health records. We also extracted the hospital course, outcomes, and complications.

2.4. Statistical analysis:

Categorical variables (i.e., gender, occupation, nationality, smoking history, presenting complaints, CXR findings, treatment) were studied utilizing the chi-square test and logistic regression models. The SPSS software (version 25, IBM Corp.) was used for statistical analysis. Simple univariate logistic regression was

applied to obtain associations, and a P value of < 0.05 was considered significant. A multivariate analysis was carried out using significant variables from univariate analysis to determine significant variables.

3. Results:

3.1 Demography

Between March 15 and August 31, 2020, 16,974 adult patients were tested for SARS-CoV-2 by RT-PCR at KSUMC, Riyadh. Of those patients, 3,481 (20.50%) were SARS-CoV-2 positive (Figure 1). Of the positive cases, 744 (21.37%) were hospitalized, and one patient was transferred to another hospital and was excluded from further analysis. Thus, 743 patients were included in the study and reached an outcome of either discharge or in-hospital mortality. Among these patients, 459 (62%) were male, and 284 (38%) were female. The median age was 53 years, with an interquartile range of 24 (39–63), and 572 (77%) were below the age of 65 years. Among these patients, 56% were Saudi nationals, and 7% were HCWs. Underlying medical conditions included obesity in 43%, diabetes mellitus (DM) in 42%, and HTN in 40% (Table 1).

The source of SARS-CoV-2 infection was not identified in 58% of cases, whereas close contact with SARS-CoV-2-infected individuals was reported in 26%. Only 0.4% involved travel-related infections.

3.2 Clinical presentations:

Fever was the most common presentation (66%, *n*=489), followed by dyspnea (62%, *n*=462), cough (60%, *n*=447), diarrhea and/or vomiting (36%, *n*=266), and easy fatiguability (25%, *n*=185). Most patients presented to a hospital within 7 days of symptom onset (*n*=480, 65%). In relation to the severity of the disease, the disease was critical in 19%, severe in 17%, and mild/moderate in 42%, and 11%

had URTI. The remaining 11.7% had asymptomatic infections and tested positive during active screening strategy. Among the patients, 104 (14%) were directly admitted to the ICU, and the remaining 639 (86%) were admitted to the general ward. From the total cohort, 281, 263, and 264 underwent testing for MERS-CoV, influenza A, and influenza B, respectively, via PCR. None were positive, indicating no co-infection with these viruses in the tested cohort.

3.3 Factors associated with poor outcomes (univariate analysis):

By the end of the study period, 117 (15.7%) had died. The association of different risk factors with mortality was tested using univariate analysis. Significant risk factors were old age (≥ 65 years), non-HCW, and the presence of comorbidity. Age was not a significant risk factor for IMV or ICU admission. The presence of lung infiltration as shown in chest X-ray upon hospital admission was significantly associated with mortality (p value <.001, *OR 2.5, 95% CI [1.5–4.1]*).

Clinical and laboratory risk factors in relation to ICU admission, IMV, or mortality are detailed in Table 2.

3.4 Factors associated with poor outcomes (multivariate analysis):

All significant factors in univariate analysis were reanalyzed using multivariate logistic regression with each poor outcome, namely, mortality, IMV, and ICU admission. The analysis showed that an initial respiratory rate of > 24/min (P=.031, *OR 2.8, 95% CI [1.1–7.2]*), a systolic blood pressure (SBP) of < 90 mmHg (P=.041, *OR 6.0, 95% CI [1.1–34.0]*) in the first 24 hours of presentation, and a lymphocyte count of <1 $\times 10^9$/L (P=.020, *OR 2.9, 95% CI [1.2–7.2]*) and an aspartate transaminase (AST) level of > 37 units/L (P=.026, *OR 3.3, 95% CI [1.2–*

9.4]) in the first 48 hours of presentation were independently associated with mortality.

An SBP of < 90 mmHg and an AST level of > 37 units/L were also independent risk factors for ICU admission. An RT-PCR Ct value of ≤ 24 in the first positive RT-PCR was the only risk factor for IMV in the multivariate analysis.

4. Discussion:

In this study, we described the clinical presentations and outcomes of patients with COVID-19 who required ICU admission. In addition, we examined the risk factors associated with poor outcomes of death, ICU admission, and IMV. Most of our patients were male, accounting for 61.8% of the study population. A similar finding was observed in a systematic review and meta-analysis showing that among 13,654 patients, 8,557 (62.6%) were male[16]. Approximately 77% of our patients were younger than 65 years. The finding that younger adults represent the majority of hospitalized patients with COVID-19 was also found by another local study from a center in the capital of Saudi Arabia, where 66% of patients were younger than 60 years[17]. The median age of our patients was 53 years, which is similar to a systemic review of six studies conducted in China, where the median age was 55.5 years[18]. Of the included patients, 42.5% were obese (i.e., with a BMI of ≥ 30), which is much less than the result in a case series of 463 patients in Detroit, US (58%)[19] and greater than the result observed by Argenziano MG et al. (36.3%)[20].

Importantly, the most prevalent chronic disease was DM at 42%, followed by HTN at 40%. Active cancer and autoimmune diseases were not prevalent in our study population, which is different from a retrospective case series in Spain that included 1,549 patients; the study showed that 55% of patients hospitalized with

COVID 19 had HTN, 45% had a history of cerebrovascular disease, and only 24.8% had DM[21]. Another retrospective study in New York, USA showed that among 1000 patients with COVID-19, 57% had HTN, and 34.3% had DM[20]. These findings may suggest the increasing prevalence of DM in Saudi Arabia; a recent report in KSA showed that 48% of admitted patients had DM which is almost similar to our finding [22]. Although no definite risk was significantly associated with blood type, the most frequent blood group (41%) in our study population of 743 hospitalized patients was ABO group O (Rh +\-). This finding was different from an observation in a case control study that included over 1000 Iraqi patients, where blood group A (Rh +\-) was the most common[23].

Pregnant women with COVID-19 infection comprised 14.8% of our population, which is similar to a reported analysis of COVID-19 cases in the UK[24]. The majority of the patients included in this study did not report a specific epidemiological link of COVID-19 infection acquisition, and only 26% reported contact with a confirmed case. This finding is different from the reported results of a study in Wuhan, China, where 92% of patients reported contact with a confirmed case[25]. The lack of any known contact may be attributed to unrecognized asymptomatic transmission[26, 27].

Fever was the most reported symptom, followed by dyspnea and cough. Only 6.7% of the patients presented with anosmia, which was the least reported symptom. This result is consistent with the results of a systemic review and meta-analysis by Mesas et al.[5] and with studies in the US, UK, Turkey, and China[20, 24, 28, 29]. However, in one study that included data from 18 European hospitals, headache, anosmia, and nasal obstruction were the most reported symptoms[30]. The duration of symptoms was less than 7 days in most of our patients, which is similar to the reported duration of illness in a study in Wuhan, China[31]. This result can

be explained by most of our patients having mild to moderate disease. Patients with URTI or with asymptomatic infection were mainly admitted for other reasons (e.g., delivery). A majority of the patients were admitted to COVID-19 wards, with only 14% requiring direct ICU admission with an overall median length of hospital stay of 8 days. One study conducted in New York showed a higher percentage of ICU admissions (23.6%) with an overall median length of stay of 6 days[20]. The case fatality ratio (CFR) in our study was 15.7%, whereas those in two studies conducted in the US were 21.1% and 21%[20, 32]. A study in Wuhan, China, showed an overall CFR of 28.27%[25]. A study in the UK including 20,133 patients showed a CFR of 26% with a median age of 80 years[24]. Our cohort was consistent with previous studies citing age as an important predictor of mortality[33, 34].

Serum lactate was identified as a risk factor for the need for IMV in our study. Chen et al. showed that high serum lactate was found in mechanically ventilated patients; however, it was not adjusted to other factors[35]. Inconsistent with our study, that of Wang et al. showed an association between serum lactate and mortality, with an odds ratio of 2.6[36]. Most of our cohort did not have a lactate level upon admission, as it was analyzed only when the patient deteriorated, which may explain its association with the need for IMV.

Our univariate analysis showed that D-dimer and creatinine were associated with mortality, ICU admission, and the need for IMV. Figliozzi et al. have demonstrated in a meta-analysis of > 3,000 patients that higher D-dimer is associated with death, ICU admission, and/or IMV[16]. A study in Brazil that identified predictors of poor outcome showed that a creatinine level of >105 μmol/L is significantly associated with all three outcomes. Consistent with our cohort, their multivariate analysis showed that creatinine level was not associated with mortality[33].

Our cohort did not show a poor outcome associated with gender, similar to other studies[33, 37]. On the contrary, a meta-analysis of > 600,000 patients showed significantly worse outcomes with male gender; however, this result was not adjusted to other patients' characteristics[16].

A striking feature of our study is that BMI was not significantly associated with poor outcome. Obesity prevalence in Saudi Arabia is approximately 35%[38], and that in our cohort was slightly higher. A meta-analysis of >10,000 patients showed poor outcomes associated with obesity, with a pooled OR of 1.88[39]. Obesity prevalence in that meta-analysis was 33%, which was less than that in our cohort. In addition, in this meta-analysis, studies from the USA that has an age-adjusted prevalence of obesity of 42.4%[40], which is almost similar to Saudi Arabia at 38.3%[41], did not show statistically significant obesity risk.

Smoking prevalence in Saudi Arabia has a median of 16.5% among students, 22.6% among adults, and 25% among the those above 65 years of age[42]. However, our cohort showed a much lower rate of only 4.4%, these differences may be due to the cited study being conducted more than a decade ago, since then, in 2017, a 100% excise tax on tobacco products was enforced which led to a significant reduction in smoking in the country[43]. A meta-analysis of 19 studies showed a progression of COVID-19 in patients with a history of smoking (OR 1.91)[44].

Our study did not show any association between poor outcome and ABO blood group. A meta-analysis of five studies showed a slightly increased association between mortality in patients with COVID-19 and blood group A[45]. Our institute performs blood grouping in patients that receive blood or blood products; hence, half of our patients had no documented blood group.

Furthermore, consistent with other studies[46, 47], the use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers was not associated with any changes in COVID-19 progression.

Cerebrovascular diseases, active malignancy, and lung diseases are linked to increased morbidity and mortality in patients with COVID-19[16]. However, our cohort did not show a similar association. This result may be due to a younger cohort, which has a lower prevalence of diseases compared with older populations.

A recent meta-analysis of > 5,000 patients showed that in contrast with dyspnea, cough and gastrointestinal (GI) symptoms were not associated with higher mortality[5]. In another meta-analysis, presence of diarrhea on presentation was associated with more severe disease with an odd ratio of 1.63 (95% CI: 1.11-3.38) compared to those who did not have diarrhea [39]. A median duration of symptoms of 5 days has been associated with higher mortality [40]. By contrast, a study in China showed that COVID-19 survivors and non-survivors showed a similar median duration of 11 days[25]. Our study did not show a significant association between cough, GI symptoms, or the duration of symptoms and poor outcome.

Using multivariate logistic regression, we identified several clinical and laboratory predictors of poor outcomes. Although a cut-off value of 30 breaths/min is considered one of the criteria for severe disease as per the Saudi Ministry of Health guidelines[15], we found that a lower value of >24 breaths/min is an independent risk factor associated with mortality. A study in South Florida showed an OR of 2.54 for ICU admission and death using multivariate analysis [41]. A similar study in Louisiana showed a hazard ratio of 2 for in-hospital death with a respiratory rate of >24 breaths/min[34] .

We report low SBP as an additional risk factor for mortality. A study in New York including > 6,000 patients admitted showed that hypotension is associated with mortality (HR: 1.38 [1.06–1.8]) [42].

Lymphopenia has been studied as a potential predictor of poor outcome in multiple publications. In one prospective study, lymphopenia had no effect outcomes [43]. A large meta-analysis that included >20,000 patients[16] showed that lymphocytopenia was associated with an increased risk of mortality in hospitalized patients with COVID-19. Our study also showed that it is an independent risk factor for mortality, showing an OR of 2.9.

AST is a marker for liver function. A meta-analysis of 21 studies showed that elevated AST, especially in the older population, is associated with increased mortality (effect size: 1.61)[5]. A study in China showed that AST is more related to mortality compared with other liver enzymes (HR of 4.81 if AST is between 40 and 120 U/L) [44]. Another meta-analysis of four studies showed an OR of 2.53 for ICU admission with elevated AST [42].

As with other viral illnesses, such as HIV, Ebola, and influenza, SARS-CoV-2 viral load is associated with disease severity and progression [45]. Reinforcing findings in recent reports [46], our study showed a significant association between high viral load and the need for IMV, with a Ct value of ≤ 24 serving as an independent predictor for the need for IMV and indicating more severe disease.

Our study has several limitations. Given that this work is a retrospective study from a single center, not all patients were tested for all inflammatory markers, and the effect of therapeutic measures was not studied.

In conclusion, variable factors were identified as predictors of different outcomes among COVID-19 patients in a MERS-CoV referral hospital. A low initial Ct value of SARS-CoV-2 PCR predicted IMV. The presence of tachypnea, hypotension, lymphopenia, and elevated AST in the first 48 hours of presentation were independently associated with mortality. This study provides possible independent predictors of mortality and IMV. The data may be helpful in the early identification of high-risk patients with COVID-19. Large prospective studies are warranted to validate these results.

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Figure 1: Diagram showing the study population and outcomes

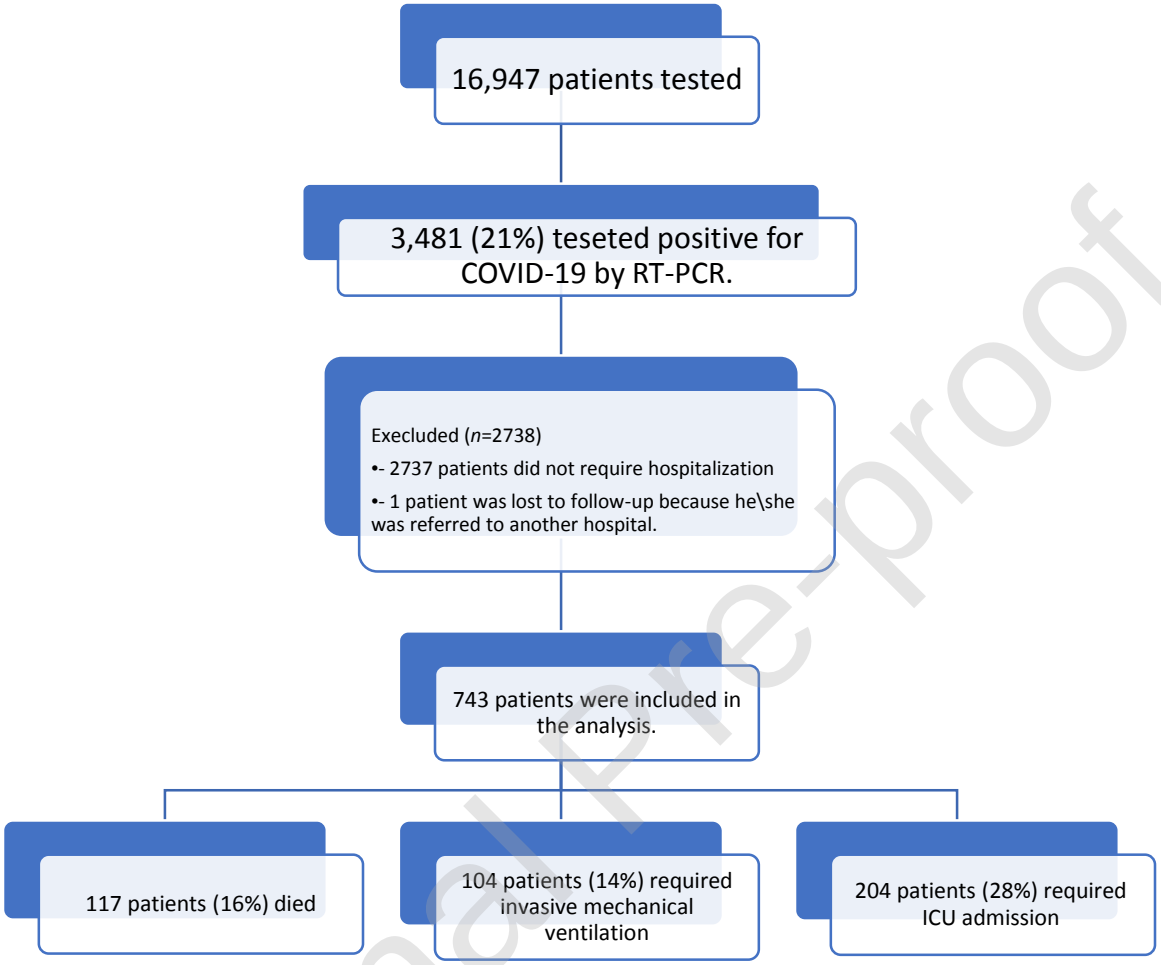

Table 1: Demographic and clinical characteristics of 743 hospitalized patients with SARS-CoV-2 at King Saud University Medical City

		(*n*)	(%)
Gender	Female	284	38.2
	Male	459	61.8
Age	< 65 years	572	77
	≥ 65 year	171	23
Median age (IQR)	53 (39–63)		
Occupation	HCWs	52	7
	Non-HCWs	691	93
Nationality	Saudi Nationals	423	57
	Arab countries nationals	116	16
	Indian Subcontinent nationals.	85	11
	Other countries nationals.	119	16
BMI, kg\m2	Obese (≥ 30)	316	42.5
	Overweight (25–29.9)	220	29.6
	Normal (18.5–24.9)	143	19.2
	Underweight (< 18.5)	13	1.7
	NA (not documented)	51	6.9
Smoking	Active or former smoker	33	4.4
	Life-time non-smoker	674	90.7
	NA (not documented)	36	4.9
Comorbid conditions	Diabetes mellitus	308	41.5
	Hypertension	295	39.7
	Dyslipidemia	104	14
	Ischemic heart diseases	72	9.7
	Lung Diseases*	63	8.5
	Heart failure	50	6.7
	Chronic kidney disease	44	5.9
	Hypothyroidism	41	5.5
	Stroke	27	3.6
	Autoimmune diseases	18	2.4
	Active cancer	17	2.3
Pregnancy	Yes	42	14.8
	No	242	85.2
Blood group	A (Rh +/-)	100	32
	B (Rh +/-)	71	22.8
	AB (Rh +/-)	13	4.2
	O (Rh +/-)	128	41
	NA (not documented)	431	
Epidemiological link	Travel history to a country with SARS-CoV-2 cases	2	0.3
	Close contact with confirmed SARS-CoV-2 cases	193	26

	Visit to a healthcare facility within 14 days	116	15.6
	Not identified	432	58.1
Presenting complaints	Fever	489	65.8
	Dyspnea	462	62.2
	Cough	447	60.2
	GI Symptoms Diarrhea (*n*=116, 44%) Other GI symptoms (*n*=150, 56%)	266	35.8
	Fatigue	185	24.9
	URTI symptoms	120	16.2
	Headache	77	10.4
	Anosmia	50	6.7
	Asymptomatic	87	11.7
Duration of symptoms	7 days or less	480	64.6
	More than 7 days	176	23.7
	NA (not applicable)	87	11.7
Severity**	Critical disease	141	19
	Severe disease	123	16.5
	Mild/moderate disease	312	42
	URTI	80	10.8
	Asymptomatic	87	11.7
Initial admission site	Intensive care unit	104	14
	Ward	639	86
First poor outcome	Death	117	15.7
	Discharge	626	84.3
Median length of stay (IQR): 8 days (4–15 days)			
Second poor outcome	IMV need	103	13.9
	No IMV need	640	86.1
Median MV days (IQR):	8 days (4–19 days)		
Third poor outcome	ICU admission	204	27.5
	No ICU admission	539	72.5
Median ICU days (IQR):	8 days (5–16 days)		

HCWs; healthcare workers, GI; gastrointestinal, URTI; upper respiratory tract infection, ICU; intensive care unit, IMV; invasive mechanical ventilation.

* Including chronic obstructive pulmonary disease, bronchial asthma, interstitial lung disease, obstructive sleep apnea–obesity hypoventilation syndrome, and bronchiectasis.

** According to the Saudi Ministry of Health protocol for patients suspected of or confirmed to have COVID-19[9]

Table 2: Predictors of poor outcomes among hospitalized patients with SARS-CoV-2 infection at King Saud University Medical City using univariate analysis.

	Univariate OR (95% CI) **(For mortality)**	*P*	Univariate OR (95% CI) **(For invasive mechanical ventilation)**	*P*	Univariate OR (95% CI) **(For ICU admission)**	P
Demographic data						
Gender	-	.441	-	.340	-	.091
Age ≥ 65 years (vs. < 65 years)	2.5 (1.6–3.8)	< .001	-	.279	-	.077
Non-HCWs (vs. HCWs)	10.3 (1.4–75.2)	.005	8.8 (1.2–64.6)	.010	10.3 (2.5–42.9)	< .001
BMI	-	.170	-	.501	-	.220
Smoking history	-	.077	-	.064	-	.084
Blood group	-	.817	-	.773	-	.582
Past medical history (each against no history of that disease)						
Presence of ≥ 1 comorbidities (vs. none)	2.9 (1.8–4.8)	< .001	2.0 (1.3–3.2)	.003	1.9 (1.3–2.7)	< .001
Use of ACEis or ARBs (vs. no use)	-	.266	-	.928	-	.364
Hypertension	2.7 (1.8–4.0)	< .001	1.8 (1.2–2.8)	.004	1.8 (1.3–2.5)	< .001
Diabetes mellitus	2.2 (1.5–3.3)	< .001	1.8 (1.2–2.8)	.004	1.8 (1.3–2.5)	< .001
Heart failure	2.5 (1.3–4.7)	.004	-	.381	2.4 (1.4–4.3)	.002
Stroke	-	.415	-	.249	-	.486
Chronic kidney disease	2.1 (1.1–4.3)	.030	-	.192	1.9 (1.0–3.6)	.039
Dyslipidemia	2.1 (1.3–3.5)	.002	-	.088	-	.078
Any lung disease*	-	.066	-	.213	-	.836
Autoimmune disease	-	.753	-	.731	-	.968
Hypothyroidism	-	.810	-	.541	-	.530
Active cancer	-	.166	-	.800	-	.582
History and vital signs in the first 24 hours						
History of fever (vs. no fever)	-	.189	-	.148	-	.051
History of dyspnea (vs. no dyspnea)	1.9 (1.2–3.0)	.005	2.3 (1.4–3.7)	.001	2.5 (1.7–3.6)	< .001
History of Cough (vs. no cough)	-	.571	-	.357	-	.432
History of Anosmia (vs. no Anosmia)	-	.473	-	.726	-	.833
History of GI symptoms (vs. no GI symptoms)	-	.414	-	.391	-	.603
Symptoms duration less than 7 days (vs. ≥ 7 days)	2.6 (1.5–4.6)	< .001	1.8 (1.0–3.0)	.037	-	.321
Initial temperature of ≥ 38°C	1.6 (1.0–2.2)	.031	1.6 (1.1–2.5)	.026	1.5 (1.0–2.0)	.030

(vs. below 38)						
Initial systolic blood pressure < 90 mmHg (vs. ≥ 90 mmHg)	4.1 (2.0–8.4)	< .001	4.9 (2.4–10.0)	< .001	3.2 (1.6–6.3)	.001
Initial respiratory rate > 24 breaths/min (vs. ≤ 24 breaths/min)	2.9 (1.9–4.3)	< .001	3.6 (2.3–5.5)	< .001	5.0 (3.5–7.0)	< .001
Initial oxygen saturation below 94% (vs. ≥ 94%)	1.9 (1.3–2.9)	.002	2.2 (1.4–3.4)	< .001	3.0 (2.1–4.2)	< .001
Laboratory and radiological findings in the first 48 hours						
RT-PCR Ct value ≤ 24 (vs. > 24)	1.8 (1.2–2.7)	.004	1.7 (1.1–2.6)	.018	-	.072
White blood cell counts of < 4 × 10^9 cells/L (vs. ≥ 4 × 10^9 cells/L)	-	.471	-	.756	-	.460
Lymphocytes count less than 1 × 10^9 cells/L (vs. ≥ 1× 10^9 cells/L)	3.7 (2.5–5.7)	< .001	4.8 (3.0–7.6)	< .001	4.2 (3.0–6.0)	< .001
Platelets count less than 150 × 10^9 cells/L (vs. ≥ 150 × 10^9 cells/L)	-	.293	-	.161	-	.292
D-dimer > 0.45 mg/dl (vs. ≤ 0.45 mg/dl)	2.2 (1.0–4.6)	.044	2.7 (1.1–6.3)	.021	2.3 (1.3–4.0)	.005
AST > 37 units/L (vs. ≤ 37 units\L)	3.4 (2.1–5.3)	< .001	3.7 (2.2–6.0)	< .001	3.0 (2.0–4.2)	< .001
ALT > 61 units/L (vs. ≤ 61 units/L)	-	.627	1.6 (1.0–2.6)	.035	1.5 (1.0–2.2)	.028
Creatinine > 115 µmol/L (vs. ≤ 115)	3.9 (2.5–6.0)	< .001	3.2 (2.0–5.0)	< .001	2.8 (1.9–4.1)	< .001
Ferritin > 400 µg/L (vs. ≤ 400 µg/L)	1.6 (1.0–2.4)	.037	2.4 (1.5–4.0)	< .001	2.3 (1.6–3.4)	< .001
CRP > 20 mg/L (vs. ≤ 20 mg/L)	4.3 (1.7–10.8)	.001	4.0 (1.6–10.0)	.002	2.5 (1.4–4.4)	.001
PCT > 0.5 ng/ml (vs. ≤ 0.5 ng/ml)	2.3 (1.2–4.4)	.008	2.0 (1.1–3.8)	.029	2.3 (1.5–3.8)	< .001
Trop I > 100 ng/L (vs. ≤ 100 ng/L)	2.6 (1.3–5.2)	.006	2.8 (1.4–5.6)	.003	2.9 (1.5–5.7)	.001
CK > 308 units/L (vs. ≤ 308 units/L)	2.0 (1.2–3.4)	.006	2.3 (1.4–3.8)	.001	1.6 (1.1–2.5)	.030
Lactate > 2 mmol/L (vs. ≤ 2)	-	.080	1.9 (1.1–3.1)	.014	-	.075
IL-6 > 7 pg/ml (vs. ≤ 7)	-	.052	-	.262	-	.390
CXR infiltrates (vs. no infiltrates)	2.5 (1.5–4.1)	< .001	3.0 (1.7–5.2)	< .001	3.0 (2.0–4.4)	< .001

HCWs; healthcare workers, RT-PCR; reverse transcription-polymerase chain reaction, ct; cycle threshold, AST; aspartate transaminase, CRP; C-reactive protein, PCT; procalcitonin, Trop I; troponin I, CK; creatinine kinase, CXR; chest X-ray, BMI; body mass index, ACEIs; angiotensin converting enzyme inhibitors, ARBs; angiotensin receptor blockers, GI; gastrointestinal, ALT; alanine transaminase, IL-6; interleukin-6, ICU; intensive care unit

* Including chronic obstructive pulmonary disease, bronchial asthma, interstitial lung disease, obstructive sleep apnea-obesity hypoventilation syndrome, and bronchiectasis.

Table 3: Multivariate analysis of predictors of poor outcomes (mortality, invasive mechanical ventilation, ICU admission) among hospitalized patients with SARS-CoV-2 infection at King Saud University Medical City

	Multivariate OR (95% CI)	*P*
Predictors of mortality		
Initial respiratory rate > 24 breaths/min (vs. ≤ 24 breaths/min)	2.8 (1.1–7.2)	.031
Initial systolic blood pressure < 90 mmHg (vs. ≥ 90 mmHg)	6.0 (1.1–34.0)	.041
Lymphocyte count < 1 × 10^9 cells/L (vs. ≥ 1 × 10^9 cells/L)	2.9 (1.2–7.2)	.020
AST > 37 units/L (vs. ≤ 37 units/L)	3.3 (1.2–9.4)	.026
Predictors of invasive mechanical ventilation		
RT-PCR Ct value ≤ 24 (vs. > 24)	2.5 (1.1–5.4)	.023
Predictors of ICU admission		
Initial systolic blood pressure < 90 mmHg (vs. ≥ 90 mmHg)	5.9 (1.2–30.0)	.032
AST > 37 units/L (vs. ≤ 37 units/L)	3.1 (1.2–8.5)	.024

RT-PCR; reverse transcription-polymerase chain reaction, Ct; cycle threshold, AST; aspartate transaminase.